# Methods

## *Patients and Centers*

Adult patients with mastocytosis participated in this multicenter prospective double-blind placebo-controlled trial at three centers in Switzerland (Zurich, Berne, and Geneva) between 2009 and 2015. The study was approved by the local ethics committees and was conducted according to the Declaration of Helsinki. The study is registered at ClinicalTrials.gov NCT01333293.

Patients with histologically confirmed systemic or cutaneous mastocytosis were screened for this trial. Inclusion criteria were the following: histologically approved mastocytosis (systemic or cutaneous), diagnosis confirmed by a bone marrow, skin, or other biopsy, and age between 18 and 70 years. Exclusion criteria were: age <18 years, allergy to omalizumab or another ingredient, malignant tumor in the past 5 years, severe infections including HIV, active tuberculosis or being under tuberculostatic treatment, immunosuppressive treatment, pregnancy or lactation, or refusal to participate in the study for other reasons. All patients included signed informed consent.

After a run-in-period of 2 months, patients were randomized to either the omalizumab group or the placebo group. Omalizumab (Xolair®) was dosed according to the total serum IgE and body weight as in allergic asthma omalizumab (dose in the patient cohort 150 or 300 mg/injection). Injections were performed subcutaneously at the study visits once monthly for a period of 6 months with a total of 7 injections. After the treatment phase, an early follow-up visit followed 1 month after the last injection of the study drug and a late follow-up 4 months after the last injection of the study drug.

## *Assessments*

Throughout the study, the AFIRMM score [19, 20] was collected at most of the monthly visits as well as at the early and late follow-ups. In parallel, patients kept a diary of itching and up to five individual main complaints, each with a score ranging from 1 to 10. The primary endpoint of this study was the change in the AFIRMM score between baseline at randomization and after 6 months of treatment. At recruitment start, the AFIRMM score was the only internationally published scoring system for symptoms due to mastocytosis. The score includes 38 complaints potentially associated with mastocytosis, which are summed in severity-dependent weighting. Secondary endpoints included the amount of allergic/anaphylactic reactions, intake of mastocytosis-specific medication, symptom scores for main complaints (analog score 1–10) and itching, specific serologic investigations such as tryptase, FcεR (Fc-epsilon receptors), as well as safety parameters like adverse events and local reactions.

## *Laboratory Markers*

Total IgE and tryptase were determined in all patients at the beginning of the study by routine methods (Thermo Fisher diagnostics). Determination of tryptase was repeated in the course of the study during and after therapy with omalizumab. FcεRI expression was measured in the ADR-AC laboratory in Berne, Switzerland.

## *Statistical Analysis*

All study data were collected by eCRF (secuTrial©). The absolute difference of the AFIRMM score between baseline and visit 8 and visit 9/11, respectively, was analyzed using the exact Mann-Whitney U test. Statistical analyses were done using SPSS Version 20. Figures were done with GraphPad Prism Version 5.